REMARKS

Claims 9-12, 20-22, 24-26, 28-32, and 34-36 are pending in the application, with claim 9 being currently amended.

Claim 9, which is the only independent claim, has been amended to more clearly define over the art of record. In particular, claim 9 now recites a process for producing lactoperoxidase comprising, in part, a step (4) for concentrating said leaching solution through an ultrafiltration membrane so that a protein content in said concentrated leaching solution becomes 0.9 to 15% to thereby effect precipitation of proteins other than lactoperoxidase in the concentrated leaching solution which is retentate, wherein the precipitation is not re-dissolved in purified water. Support for the amendments can be found throughout the application and at least at page 16, lines 27-29; page 17, lines 9-15; and page 21, lines 13-15, for example.

35 U.S.C. §103 rejections

In the Official Action, Examiner continues to reject previously pending claims 9-12, 20-22, 24-26, 29-32, and 34-36 under 35 U.S.C. 103(a) as being unpatentable over Uchida U.S. Patent No. 5,516,675 ("Uchida"), Burling U.S. Patent No. 5,149,647 ("Burling"), Kussendrager U.S. Patent Nos. 6,010,698 and 5,596,082 ("the Kussendrager '698 patent" and "the Kussendrager '082 patent", respectively) (collectively, "the Kussendrager patents"), Souppe FR 2841747 (as evidenced by U.S. Patent No. 7,247,331) ("Souppe"), and Lihme U.S. Patent No. 5,780,593 ("Lihme"). *See* Official Action at Pages 3-7. Applicants respectfully disagree with the present rejections, particularly in view of independent claim 9 as currently amended.

In the present invention, an eluting treatment of a cation exchanger, in which a specific leaching solution having specific ionic strength is used, and a concentration treatment, in which a concentration of protein to the specific range is conducted by ultrafiltration method, are

combined. Due to the combination, unexpected excellent effects are achieved such that, as shown in step (4), when a leaching solution is concentrated through an ultrafiltration membrane to achieve 0.9 to 15% of a protein content, a precipitate of proteins other than lactoperoxidase is formed in the leaching solution (retentate). And while the precipitate of proteins other than lactoperoxidase is formed as a solid in the concentrated leaching solution, lactoperoxidase is dissolved in the concentrated leaching solution. Furthermore, the precipitate formed in step (4) can be easily collected and removed in step (5). In this way, the ultrafiltration treatment of the present invention makes it possible to generate a precipitate of protein impurities, which are different from lactoperoxidase, in a concentrated leaching solution.

Further to that end, after the ultrafiltration treatment, it is possible to obtain a solution including lactoperoxidase at a high concentration merely by removing the precipitate (precipitate of proteins other than lactoperoxidase) from the concentrated leaching solution. After removing the precipitate, it is also possible to obtain high purity lactoperoxidase by drying the solution from which the precipitate has been removed. Furthermore, the generated precipitate is no longer dissolved even if purified water, or the like, is added to the concentrated solution including a precipitate of proteins other than lactoperoxidase, and even if subsequent concentration is further conducted by ultrafiltration after said addition of purified water, or the like. The excellent characteristic of the present invention enables easy performance of a desalting treatment. See, e.g., page 21, lines 16-18 of the present specification.

Applicants now specifically address the present §103 rejections. Even assuming *arguendo* that one skilled in the art would combine Uchida, Burling, the Kussendrager patents, Souppe, and Lihme, which we assert one would not, the combination still fails to make obvious Applicant's process for producing lactoperoxidase, as now recited in claim 9. Indeed, to establish

prima facie obviousness of a claimed invention, it is certainly well established that all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974); *See also* MPEP §2143.03 (citing *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970))(To establish *prima facie* obviousness of a claimed invention, it is certainly well established that "all words in a claim must be considered when judging the patentability of that claim against the prior art or suggested by the prior art." (emphasis added)). In the instant case, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness for the reasons that follow.

Again, claim 9 now requires a step (4) for concentrating said leaching solution through an ultrafiltration membrane so that a protein content in said concentrated leaching solution becomes 0.9 to 15% to thereby effect precipitation of proteins other than lactoperoxidase in the concentrated leaching solution which is retentate, wherein the precipitation is not re-dissolved in purified water.

Upon review of Uchida, this reference discloses that an ultrafiltration method is performed but there is no disclosure or suggestion that the ultrafiltration method is used to separate, via precipitation, lactoperoxidase, as a soluble fraction, from impurities, as an insoluble fraction. See col. 6, lines 12-18. In support thereof, Uchida states:

> The isolation and purification of lactoperoxidase, secretory component, and lactoferrin by the present invention, requires no repeated chromatographic isolation and purification procedures and can be performed by simple methods. That is, the present invention gave lactoperoxidase, secretory component, and lactoferrin at purity of 80% or over in a single chromatographic treatment. Additional treatment with an ultrafiltration eliminates a small amount of low molecular weight fraction and provides lactoperoxidase, secretory component, and lactoferrin at purity of 85% or over. The simplified process provides not only highly pure lactoperoxidase, secretory component, and lactoferrin at high yield

> but also reduces production cost. The products can be used for foods and pharmaceuticals for the treatment and prevention of infectious diseases and anemia." Emphasis added. Col. 8, lines 11-14.

To that end, the ultrafiltration methods disclosed in Uchida separate and remove components based on molecular weight by passing low molecular weight proteins through the ultrafiltration membrane. In stark contrast, in the present invention, when lactoperoxidase adsorbed into the cation exchanger is eluted into the leaching solvent, the lactoperoxidase is obtained in a mixture with other fractions (impurities). Then, when concentration is performed using an ultrafiltration membrane, the other fractions (impurities) are selectively isolated via precipitation in the retentate and removed based, thus, on differences in the solubility, not molecular weight. As a result, high purity lactoperoxidase can be obtained. See page 8, lines 5-7 of the present specification. The isolation of the present invention is carried out based on the characteristics that solubility of lactoperoxidase is different from that of proteins other than lactoperoxidase. Within a concentrated solution generated by the ultrafiltration (that is, within a solution which has not passed through an ultrafiltration membrane and exists as a retentate), lactoperoxidase (a soluble fraction) and proteins other than lactoperoxidase (a precipitation fraction) are separated. And such a separation method is neither disclosed nor suggested by Uchida.

Furthermore, after ultrafiltration, Uchida fails to take note of the solubility of the components included in a concentrated solution. For example, in Example 1 of Uchida, after concentration and desalting are conducted with an ultrafiltration membrane having a molecular weight cut-off of 10,000, lyophilization is merely performed to obtain 12 g of lactoperoxidase at a purity of 90%, 8 g of secretory component at a purity of 85%, and 17 g of lactoferrin at a purity of 95%. Based on such a disclosure, a person skilled in the art cannot come up with formation of

a precipitate of proteins other than lactoperoxidase in accordance with the solubility difference of components in the solution. In addition, a person skilled in the art is unable to discern from Uchida that, when a protein included in a leaching solution concentrated with an ultrafiltration membrane is controlled to have specific concentration, lactoperoxidase and proteins other than lactoperoxidase can be separated due to the solubility difference thereof. In this way, the present invention provides unexpected excellent effects which have not been achieved, and non-obviousness of the present invention, as embodied by independent claim 9, is evident. And the remaining references cited by Examiner fail to cure the aforementioned deficiencies.

Regarding the remaining references, i.e., Burling, the Kussendrager patents, Souppe, and Lihme, the present invention likewise provides unexpected excellent effects which have not been disclosed therein. In the present invention, due to the solubility difference between lactoperoxidase and proteins other than lactoperoxidase, a precipitate can be settled in the concentrated leaching solution by the ultrafiltration, while lactoperoxidase has been dissolved in the solution. There are no references that take note of the solubility of components in a concentrated solution obtained after ultrafiltration. Accordingly, a person skilled in the art cannot arrive at the generation of a precipitate of proteins other than lactoperoxidase using the solubility differences. Indeed, a person skilled in the art cannot arrive at the separation of lactoperoxidase and proteins other than lactoperoxidase, as is required by claim 9, since the remaining cited references fail to disclose or suggest either of controlling a protein content of a leaching solution concentrated by an ultrafiltration to a specific range or using the solubility differences between lactoperoxidase and proteins other than lactoperoxidase.

In view of all of the above, when combined, Uchida, Burling, the Kussendrager patents, Souppe, and Lihme fail to provide all of the elements of Applicants' claimed process for producing lactoperoxidase. That is, Examiner has not established a *prima facie* case of obviousness based on these disclosures. Accordingly, the rejections are overcome and must be withdrawn. Applicants, thus, respectfully submit that independent claim 9, along with its dependent claims, is allowable over the cited references.

Conclusion

As a result of the remarks given herein, Applicants submit that the rejection of the pending claims has been overcome. Therefore, Applicants respectfully submit that this case is in condition for allowance and request allowance of the pending claims.

If Examiner believes any detailed language of the claims requires further discussion, Examiner is respectfully asked to telephone the undersigned attorney so that the matter may be promptly resolved. Applicants also have submitted all fees believed to be necessary herewith. Should any additional fees or surcharges be deemed necessary, Examiner has authorization to charge fees or credit any overpayment to Deposit Account No. 23-3000.

Respectfully submitted,
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